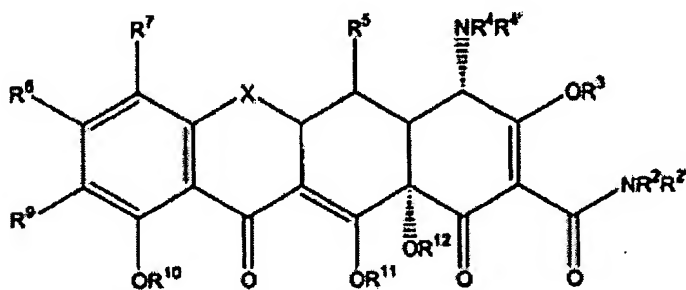


LISTING OF THE CLAIMS

This listing of claims will replace all prior versions of the claims and listing of the claims in the application. No claim amendments were made.

1. **(Previously Presented)** A substituted tetracycline compound, wherein said compound is of the formula:



(I)

wherein:

X is CR^{6'}R⁶;

R² is hydrogen;

R⁴ and R^{4'} are each alkyl;

R^{2'}, R³, R¹⁰, R¹¹ and R¹² are each hydrogen;

R⁵ is hydrogen or hydroxyl;

R⁶ and R^{6'} are each independently hydrogen or alkyl;

R⁷ is hydrogen or NR^{7c}C(=W')WR^{7a};

R⁸ is hydrogen;

R⁹ is hydrogen or NR^{9c}C(=Z')ZR^{9a};

Z is O;

Z' is O or S;

R^{9a} is substituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted

arylsulfonyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted aryl carbonyl, or substituted or unsubstituted phenyl,

wherein said substituted alkyl is substituted with halogen, amino, hydroxyl, alkoxy, alkyl carbonyloxy, alkyloxy carbonyl, aryl carbonyloxy, alkoxy carbonylamino, alkoxy carbonyloxy, aryloxy carbonyloxy, carboxylate, alkyl carbonyl, alkyl amino carbonyl, aryl alkyl aminocarbonyl, alkenyl aminocarbonyl, alkyl carbonyl, aryl carbonyl, amino alkyl, aryl alkyl carbonyl, alkenyl carbonyl, alkoxy carbonyl, silyl, aminocarbonyl, alkyl thiocarbonyl, phosphate, aralkyl, phosphonate, phosphinate, cyano, acylamino, amido, imino, sulfhydryl, alkyl thio, sulfate, aryl thio, thiocarboxylate, alkyl sulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl;

further wherein said substituted alkenyl, substituted alkynyl, substituted alkoxy substituted arylsulfonyl, substituted alkoxy carbonyl, substituted aryl carbonyl, or substituted phenyl is substituted with halogen, amino, alkyl, alkenyl, alkynyl, hydroxyl, alkoxy, alkyl carbonyloxy, alkyloxy carbonyl, aryl carbonyloxy, alkoxy carbonylamino, alkoxy carbonyloxy, aryloxy carbonyloxy, carboxylate, alkyl carbonyl, alkyl amino carbonyl, aryl alkyl aminocarbonyl, alkenyl aminocarbonyl, alkyl carbonyl, aryl carbonyl, amino alkyl, aryl alkyl carbonyl, alkenyl carbonyl, alkoxy carbonyl, silyl, aminocarbonyl, alkyl thiocarbonyl, phosphate, aralkyl, phosphonate, phosphinate, cyano, acylamino, amido, imino, sulfhydryl, alkyl thio, sulfate, aryl thio, thiocarboxylate, alkyl sulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl;

R^{9c} is hydrogen;

W is CR^{7d}R^{7e}, NR^{7b} or O;

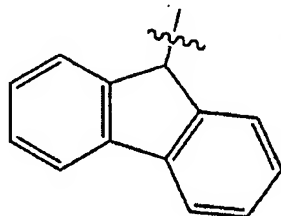
W' is O or S;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, arylsulfonyl, alkoxy carbonyl, aryl carbonyl, alkylamino, phenyl or absent;

or a pharmaceutically acceptable salt thereof, provided that R⁹ is not hydrogen when R⁷ is hydrogen.

2. (Canceled)
3. (Canceled)
4. (Previously Presented) The compound of claim 1, wherein R⁴ and R^{4'} are each methyl.
5. (Canceled)
6. (Original) The compound of claim 4, wherein R⁵ is hydrogen.
7. (Original) The compound of claim 6, wherein X is CH₂, and R⁷ is hydrogen.
8. (Canceled)

9. **(Previously Presented)** The compound of claim 4, wherein R⁵ is hydroxyl and X is CHR⁶.
10. **(Previously Presented)** The compound of claim 9, wherein R⁶ is CH₃.
11. **(Original)** The compound of claim 1, wherein R⁹ is NR^{9c}C(=Z')ZR^{9a}.
12. **(Canceled)**
13. **(Original)** The compound of claim 11, wherein Z' is oxygen.
14. **(Previously Presented)** The compound of claim 11, wherein Z' is sulfur.
- 15-18. **(Canceled)**
19. **(Previously Presented)** The compound of claim 11, wherein R^{9a} is selected from the group consisting of substituted alkyl, substituted or unsubstituted alkynyl, or substituted or unsubstituted phenyl.
20. **(Canceled)**
21. **(Previously Presented)** The compound of claim 19, wherein said substituted alkyl is substituted with one or more substituents selected from the group consisting of alkoxy carbonyl, amino, aryl carbonyl, halogen, hydroxy, alkylamino, alkoxy, or aryl.
22. **(Canceled)**
23. **(Previously Presented)** The compound of claim 19, wherein said substituted alkyl is substituted with an aryl group.
24. **(Original)** The compound of claim 23, wherein said aryl group is phenyl.
25. **(Previously Presented)** The compound of claim 19, wherein said substituted alkyl is substituted with one or more halogens.
26. **(Previously Presented)** The compound of claim 25, wherein said halogen is bromine.
- 27-29. **(Canceled)**
30. **(Previously Presented)** The compound of claim 1, wherein R^{9a} is substituted or unsubstituted phenyl.
31. **(Canceled)**
32. **(Previously Presented)** The compound of claim 11, wherein R^{9a} comprises the group:



33. (Canceled)

34. (Previously Presented) The compound of claim 30, wherein said phenyl is substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, amido, halogen, nitro, azo, alkyl sulfonyl, and arylsulfonyl.

35. (Previously Presented) The compound of claim 34, wherein said substituent is alkyl.

36. (Previously Presented) The compound of claim 35, wherein said alkyl is unsubstituted.

37. (Previously Presented) The compound of claim 35, wherein said alkyl is methyl.

38. (Previously Presented) The compound of claim 35, wherein said alkyl is substituted with one or more halogens.

39. (Previously Presented) The compound of claim 34; wherein said substituent is alkoxy and further wherein said alkoxy is methoxy.

40. (Previously Presented) The compound of claim 34, wherein said substituent is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, and amido.

41-55. (Canceled)

56. (Previously Presented) The compound of claim 1, wherein R^7 is $NR^{7c}C(=W')WR^{7a}$.

57. (Previously Presented) The compound of claim 56, wherein R^9 is hydrogen.

58. (Previously Presented) The compound of claim 57 wherein R^{7c} is hydrogen.

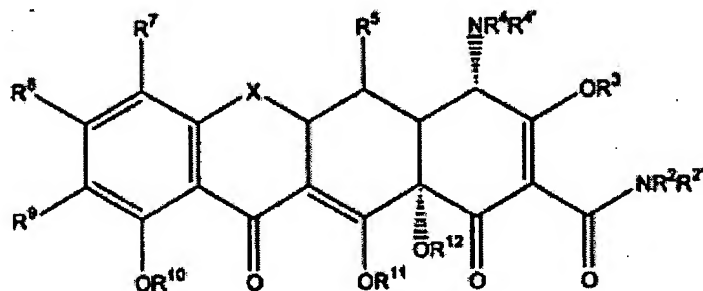
59. (Previously Presented) The compound of claim 57, wherein W' is O.

60. (Previously Presented) The compound of claim 57, wherein W' is S.

61. (Previously Presented) The compound of claims 59 or 60, wherein W is NR^{7b} .

62. (Previously Presented) The compound of claims 59 or 60, wherein W is O.

63. **(Previously Presented)** The compound of claim 57, wherein R^{7a} is selected from the group consisting of alkyl, alkenyl, alkynyl and phenyl.
64. **(Previously Presented)** The compound of claim 63, wherein R^{7a} is substituted or unsubstituted alkyl.
65. **(Previously Presented)** The compound of claim 64, wherein said alkyl is substituted with an aryl group.
66. **(Canceled)**
67. **(Previously Presented)** The compound of claim 63, wherein said phenyl is substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, amido, halogen, nitro, azo, alkyl sulfonyl, and arylsulfonyl.
68. **(Previously Presented)** The compound of claim 67, wherein said substituent is alkyl, alkoxy, or nitro.
- 69-81. **(Canceled)**
82. **(Previously Presented)** A pharmaceutical composition comprising a therapeutically effective amount of a substituted tetracycline compound and a pharmaceutically acceptable carrier, wherein said substituted tetracycline is of the formula:



wherein:

X is CR^6R^6 ;

R^2 is hydrogen;

R^4 and $R^{4'}$ are each alkyl;

$R^{2'}$, R^3 , R^{10} , R^{11} and R^{12} are each hydrogen;

R^5 is hydrogen or hydroxyl;

R^6 and $R^{6'}$ are each independently hydrogen or alkyl;

R^7 is hydrogen or $NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen;

R^9 is hydrogen or $NR^{9c}C(=Z')ZR^{9a}$;

Z is O;

Z' is O or S;

R^{9a} is substituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted arylcarbonyl, or substituted or unsubstituted phenyl;

wherein said substituted alkyl is substituted with halogen, amino, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxy, carbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxy, carbonyloxy, carboxylate, alkylcarbonyl, alkylamino, carbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonate, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl;

further wherein said substituted alkenyl, substituted alkynyl, substituted alkoxy, substituted arylsulfonyl, substituted alkoxycarbonyl, substituted arylcarbonyl, or substituted phenyl is substituted with halogen, amino, alkyl, alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxy, carbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxy, carbonyloxy, carboxylate, alkylcarbonyl, alkylamino, carbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonate, phosphinato, cyano, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl or heteroaryl;

R^{9c} is hydrogen;

W is $CR^{7d}R^{7e}$, NR^{7b} or O;

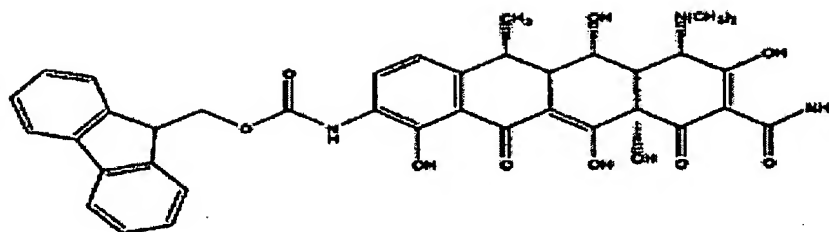
W' is O or S;

R^{7a} , R^{7b} , R^{7c} , R^{7d} , and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, phenyl or absent;

or a pharmaceutically acceptable salt thereof, provided that R^9 is not hydrogen when R^7 is hydrogen.

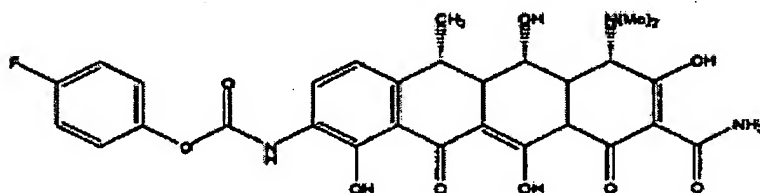
83-102. (Canceled)

103. (Previously Presented) The compound of claim 1, wherein said compound is



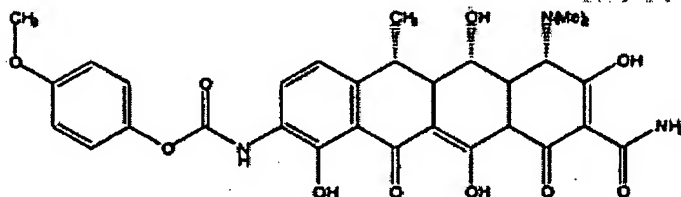
or a pharmaceutically acceptable salt thereof.

104. (Previously Presented) The compound of claim 1, wherein said compound is



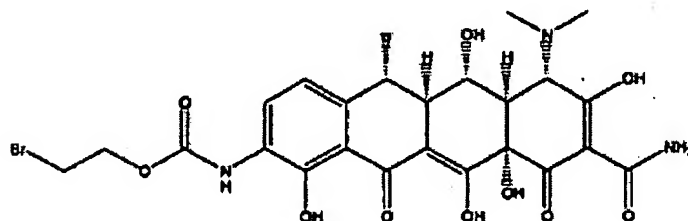
or a pharmaceutically acceptable salt thereof.

105. (Previously Presented) The compound of claim 1, wherein said compound is



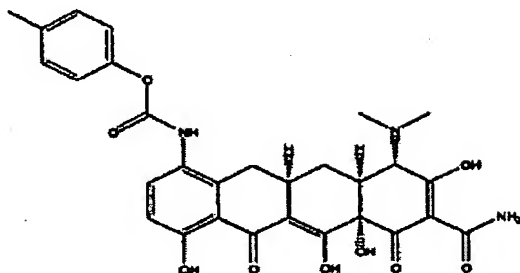
or a pharmaceutically acceptable salt thereof.

106. (Previously Presented) The compound of claim 1, wherein said compound is



or a pharmaceutically acceptable salt thereof.

107. (Previously Presented) The compound of claim 1, wherein said compound is



or a pharmaceutically acceptable salt thereof.

108. (Canceled)

109. (Previously Presented) The compound of claim 1, wherein said compound is doxycycline 9-carbamic acid 9H-fluoren-9-yl methyl ester or a pharmaceutically acceptable salt thereof.

110. (Previously Presented) The compound of claim 1, wherein said compound is Fmoc 9-amino doxycycline or a pharmaceutically acceptable salt thereof.

111. (Previously Presented) The compound of claim 1, wherein said compound is 9-(4'-fluorophenyl) doxycycline carbamate or a pharmaceutically acceptable salt thereof.

112. (Previously Presented) The compound of claim 1, wherein said compound is 9-(4'-methoxyphenyl) doxycycline carbamate or a pharmaceutically acceptable salt thereof.

113-116. (Canceled)

117. (Previously Presented) The compound of claim 1, wherein said compound is 9-(2'-bromoethyl) doxycycline carbamate or a pharmaceutically acceptable salt thereof.

118. (Previously Presented) The compound of claim 1, wherein said compound is 7-(4'-methylphenyl) sancycline carbamate or a pharmaceutically acceptable salt thereof.

119. (Previously Presented) The compound of claim 1, wherein said compound is doxycycline 7-carbamic acid 7H-fluoren-7-yl methyl ester or a pharmaceutically acceptable salt thereof.

120. (Previously Presented) The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline urea or a pharmaceutically acceptable salt thereof.

121. (Previously Presented) The compound of claim 1, wherein said compound is 7-(3-methyl-1-butyl) doxycycline urea or a pharmaceutically acceptable salt thereof.

122. (Previously Presented) The compound of claim 1, wherein said compound is 7-phenyl doxycycline urea or a pharmaceutically acceptable salt thereof.

123. (Previously Presented) The compound of claim 1, wherein said compound is 7-t-butyl doxycycline urea or a pharmaceutically acceptable salt thereof.

124. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-Fmoc amino doxycycline or a pharmaceutically acceptable salt thereof.
125. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-chloro-2-trifluoromethylphenyl) doxycycline urea or a pharmaceutically acceptable salt thereof.
126. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-fluorophenyl) doxycycline carbamate or a pharmaceutically acceptable salt thereof.
127. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-methoxyphenyl) doxycycline carbamate or a pharmaceutically acceptable salt thereof.
128. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-BOC amino doxycycline or a pharmaceutically acceptable salt thereof.
129. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline thiourea 5-propanoic acid ester or a pharmaceutically acceptable salt thereof.
130. **(Previously Presented)** The compound of claim 1, wherein said compound is doxycycline 7-thiocarbamic acid 7*H*-fluoren-7-yl methyl ester or a pharmaceutically acceptable salt thereof.
131. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline thiourea or a pharmaceutically acceptable salt thereof.
132. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(3-methyl-1-butyl) doxycycline thiourea or a pharmaceutically acceptable salt thereof.
133. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-phenyl amino doxycycline thiourea or a pharmaceutically acceptable salt thereof.
134. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-*t*-butyl amino doxycycline thiourea or a pharmaceutically acceptable salt thereof.
135. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-chloro-2'-trifluoromethylphenyl) doxycycline thiourea or a pharmaceutically acceptable salt thereof.
136. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-fluorophenyl) doxycycline thiocarbamate or a pharmaceutically acceptable salt thereof.
137. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(4'-methoxyphenyl) doxycycline thiocarbamate or a pharmaceutically acceptable salt thereof.
138. **(Previously Presented)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline urea 5-propanoic acid ester or a pharmaceutically acceptable salt thereof.

Applicants: Nelson, *et al.*
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Filing Date: February 24, 2004
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139-158. **(Canceled)**